tion of cell surface markers and for assessment of cytotoxicity. (Berd, et al., *Cancer Res.*, Vol. 46, pgs. 2572–2577 (1986)). Briefly, lymphocytes are stained with fluorescent-labeled antibodies (Leu2, Leu3, Leu4, Leu7, Leu11, Leu5, Leu9, LeuM3, HLADDR and Tac). Chromium release assays are performed with K562, Daudi autologous tumor, and allogeneic tumor targets.

To infuse the lymphocytes, they are thawed and grown for one to three additional weeks using the same procedures hereinabove described. For infusion TIL are reharvested. At the time of cell collection, one liter of saline for injection is pumped through the collection chamber and the centrifuge is stopped. Lymphocytes are resuspended in the collection bag, the centrifuge is started again, and another liter of saline is pumped through to wash fully the TIL's free of tissue culture medium components. The cells are then filtered through a platelet administration set into 600 ml transfer packs (Fenwal), and 50 ml of 25% albumin and 450,000 IU of IL-2 are added to the 200 to 300 ml volume of cells in saline. The TIL are infused over 30 to 60 minutes through a central venous catheter.

E. Administration of Interleukin-2.

The recombinant IL-2 used in this trial is provided by the Division of Cancer Treatment, National Cancer Institute (supplied by Cetus Corporation, Emeryville, Calif.) and will be administered exactly as specified in Rosenberg, et al., *New Engl. J. Med.*, Vol. 323, pgs. 570–578 (1990). The IL-2 is provided as a lyophilized powder and will be reconstituted with 1.2 ml/vial. Each vial contains approximately 1.2 mg of IL-2 (specific activity 18×10^6IV/mg). Less than 0.04 ng of endotoxin are present per vial as measured by the limulus amebocyte assay. Each vial also contains 5% mannitol and approximately 130–230 μg of sodium dodecyl sulfate/mg of IL-2. Following reconstitution the IL-2 is diluted in 50 ml of normal saline containing 5% human serum albumin, and is infused intravenously at a dose of 720,000 IU/kg over a 15 minute period every 8 hr, beginning from two to 24 hr after the TIL infusion. IL-2 will be given for up to five consecutive days as tolerated. Under no circumstances is more than 15 doses of IL-2 be administered. Doses may be skipped depending on patient tolerance. Doses will be skipped if patients reach grade III or grade IV toxicity. If this toxicity is easily reversed by supportive measures then additional doses may be given.

Patients may receive concomitant medications to control side effects. For example, the patients may be given acetaminophen (650 mg every 4 hours), indomethacin (50–75 mg every 6 hours), and ranitidine (150 mg every 12 hours) throughout the course of the treatment. Patients may also receive intravenous meperidine (25–50 mg) to control chills if they occur. Hydroxyzine hydrachloride may be given (25 mg every 6 hours) to treat pruritis, if present.

EXAMPLE 7

In this example, the procedures of Example 6 were again followed, except that the vector employed to generate vector particles and retroviral vector supernatant, was the IL-2-NeoR vector. This vector was constructed from the vector LXSN (Miller, et al, 1989), and contains the IL-2 gene. Upon construction f the IL-2-NeoR vector and the generation f vector particles and retroviral vector supernatant, the protocols for preparing gene-modified tumor cells and for treatment of patients with such cells, described in Example 6, were then followed.

Although the present invention has been described in particular with respect to genetically engineered primary human nucleated blood cells, and primary human tumor cells, it is to be understood that within the scope of the present invention, one may genetically engineer other human primary cells. Other primary human cells which may be genetically engineered in accordance with the present invention include, but are not limited to, endothelial cells, epithelial cells, keratinocytes, stem cells, hepatocytes, connective tissue cells, fibroblasts, mesenchymal cells, mesothelial cells, and parenchymal cells.

While the invention has been described with respect to certain specific embodiments, it will be appreciated that many modifications and changes may be made by those skilled in the art without departing from the spirit of the invention. It is intended, therefore, by the appended claims to cover all such modification and changes as fall within the true spirit and scope of the invention.

What is claimed is:

1. A process for providing a human with a therapeutic protein comprising:

introducing human cells into a human, said human cells having been treated in vitro to insert therein a DNA segment encoding a therapeutic protein said human cells expressing in vivo in said human a therapeutically effective amount of said therapeutic protein.

2. The process of claim 1 wherein said cells are blood cells.

3. The process of claim 1 wherein said cells are leukocytes.

4. The process of claim 1 wherein said cells are lymphocytes.

5. The process of claim 1 wherein said cells are T-lymphocytes.

6. The process of claim 1 wherein said cells are TIL cells.

7. The process of claim 1 wherein said cells are B-lymphocytes.

8. The process of any one of claims 1–7 wherein said DNA segment has been inserted into said cells in vitro by a viral vector.

9. The process of claim 8 wherein said viral vector is a retroviral vector.

10. The process of any one of claims 1–7 wherein the DNA segment encodes a cytokine.

11. The process of claim 10 wherein the cytokine is TNF.

12. The process of claim 10 wherein the cytokine is an interleukin.

13. The process of claim 10 wherein said DNA segment has been inserted into said cells in vitro by a viral vector.

14. The process f claim 13 wherein said viral vector is a retroviral vector.

* * * * *